nucleotides, 28 nucleotides, 30 nucleotides, 50 nucleotides, 75 nucleotides, 100 nucleotides and 200 nucleotides.

134. (New) The isolated nucleic acid molecule of claim 56, wherein the isolated nucleic acid molecule encodes a polypeptide which, or a fragment of which, binds a MHC receptor or an antibody.

135. (New) A host cell transformed or transfected with an expression vector of claim 60.

136. (New) A host cell transformed or transfected with an expression vector of claim 60 further comprising a nucleic acid molecule encoding a MHC molecule.

137. (New) The kit of claim 76, wherein the pair of isolated nucleic acid molecules is constructed and arranged to selectively amplify an isolated nucleic acid molecule comprising a nucleic acid molecule selected from the group consisting of (a) nucleic acid molecules which hybridize under stringent conditions to a molecule consisting of a nucleic acid sequence as set forth as SEQ ID NO:23 and which codes for a cancer associated antigen precursor, (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code, and (c) complements of (a) or (b).

REMARKS

Claims 15, 19, 41, 54, 56, 60, 62-64, 66 and 76 were pending. Claims 15, 19, 41, 54, 56, 62 and 76 have been amended. Claim 63 is cancelled herewith. Claims 122-137 have been added; these claims correspond substantially to claims 21-24, 27, 28, 44-46, 58, 59, 65, 67 and 78, respectively, as filed. No new matter has been added.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 15, 54, 56, 60, 64 and 66 under 35 U.S.C. § 112, second paragraph as "being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention."

Independent claim 15 was rejected by the Examiner as not being sufficiently clear. Th Examiner maintains that it is unclear whether the agent referred to in claim 15 acts by upwardly regulating MHC in addition to human cancer associated antigens or by increasing the amount of the cancer associated antigens that are available to be displaced. As currently written, claim 15 recites "...enriches selectively the presence of complexes of an MHC molecule and a human cancer associated antigen."

The Applicants maintain that the language of claim 15 is clear in light of the specification, which provides examples of agents useful in the practice of the claimed invention. For example, the specification recites that the agent recited by claim 15 can take a variety of forms known to one of ordinary skill in the art, including: isolated polypeptides comprising the antigen, isolated complexes of the polypeptide comprising the antigen and an HLA molecule, cells which express the isolated polypeptide comprising the antigen and cells which express both the isolated polypeptide comprising the antigen and an HLA molecule, etc. [See, e.g., page 5, lines 11-23.] Additionally, the agents encompassed by claim 15 also may include adjuvants, cytokines or other immune stimulating substances. [See, e.g., page 40, lines 5-26 and 27-33]. These are just a few examples, one of skill in the art would further recognize that the agent may also encompass compounds which facilitate and promote presentment, as well as engineered complexes of the MHC molecule and antigen peptide. Therefore, the Applicants maintain that the claim as written is sufficiently clear in light of the description provided in the specification as understood by one of ordinary skill in the art. In view of the teachings in the specification noted above, one of ordinary skill in the art will understand that the claim embraces a variety of agents, as long as the agent enriches complexes of MHC and a cancer associated antigen encoded by SEQ ID NO:23 or a structurally-related molecule.

The Examiner rejected claim 54 as being indefinite for reciting NA Group 3 molecules defined in the specification as "previously unknown nucleic acids". Claim 54 has been amended accordingly to overcome this rejection.

The Examiner has rejected claim 56 for a variety of reasons. Applicants have amended claim 56 to clarify the claim language and, additionally, provide the following arguments in response to the rejection.

The Examiner has rejected claim 56 for not being clear as to whether the proviso encompasses both parts (a) and (b). The Applicants have amended the claim to clarify that the proviso encompasses both parts (a) and (b).

The Examiner has also rejected claim 56 as relying on sequences defined by GenBank accession numbers as they are known to be updated and changed with time. Applicants disagree with the Examiner regarding the variability of information provided by GenBank accession numbers. Although GenBank is continuously updated with new sequences and changes to sequences, all changes are documented and recorded as a function of time. In addition, as of February, 1999, the "accession.version" system began in conjunction with the assignment of new GI (GenInfo Identifier) numbers. The implementation of this system provides static accession numbers with variable version numbers that increase with sequence changes. As the history of these changes are recorded and available by accession number, the use of the accession number provides access to the various versions of the sequences. Therefore, due to the historical record and system of accession.version numbers, a reference to an object in GenBank for a point in time of interest by accession number is provided that is, in fact, static rather than variable.

The Examiner has also rejected claim 56 as prolix as table 8 encompassed at least 2000 sequences. The Applicants have amended the claim to obviate the rejection.

Claim 56 was further rejected by the Examiner for the recitation of a negative limitation, which the Examiners asserts means that the claim defines what the invention is not, rather than what it is. Applicants, however, maintain that negative limitations are acceptable and are not inherently ambiguous or uncertain. According to MPEP 2173.05(1)(i), "So long as the boundaries of the patent protection sought are set forth definitely, *albeit* negatively, the claim complies with the requirements of 35 U.S.C. §112, second paragraph." As the claim specifically describes the nucleic acid molecules encompassed by the claim, with the exclusion of a sequence known as of the filing date of the priority document, the boundaries of the nucleic acid molecules of the invention are clearly and unambiguously described. The Applicants maintain that the inclusion of this negative limitation does not render claim 54 indefinite.

Finally, claim 56 was rejected by the Examiner as needing an active method step. The Applicants maintain that a method step is not needed but have amended the claim to clarify that the nucleic acid molecule of part (a) is simply described as a cancer associated antigen precursor.

Additionally, claims 15, 41, 54, 56, 62 and 76 have been amended to overcome the rejection of being vague and indefinite in the recitation of molecules which comprise non-elected SEQ ID numbers.

In view of the amendments and arguments presented above, Applicants respectfully request reconsideration of the rejections made under 35 U.S.C. § 112, second paragraph.

Rejections Under 35 U.S.C. § 102(b)

Claims 15, 19, 41, 54, 56, 60, 62, 64, 66 and 76 are rejected by the Examiner under 35 U.S.C. § 102(b) as being anticipated by Jacobs et al (WO 98/45437) as evidenced by GenBank accession number AAV88163. The Examiner maintains that Jacobs et al discloses a fragment of a Group I molecule having substitutions and deletions thereof. The Examiner argues that the sequence taught by Jacobs can be included in part (b) of NA Group 1 and 3 molecules as (b) is defined as deletions, additions and substitutions of a cancer associated antigen precursor, i.e., the nucleic acid molecule of the sequence as set forth as SEQ ID NO:23. Additionally, the Examiner maintains that the sequence of Jacobs et al is a fragment of a NA Group 1 molecule as set forth in SEQ ID NO:23.

As amended, claims 15, 41, 54, 56, 62 and 76 do not include part (b). Additionally, the sequence taught by Jacobs et al is, in fact, not a fragment of SEQ ID NO:23 as Jacobs' sequence includes several differences in nucleotide sequence relative to SEQ ID NO:23 at the end of the portion of the sequence that was compared. Therefore, as the sequence taught by Jacobs et al is not encompassed by amended claims 15, 41, 54, 56, 62 and 76, Applicants respectfully request that the Examiner withdraw the rejection of these independent claims and their respective dependent claims.

Claims 54, 56, 60 and 64 have also been rejected under 35 U.S.C. § 102(b) as being anticipated by GenBank Accession Number AI024421 as evidenced by Ono et al. The Examiner maintains that AI024421 teaches a complementary sequence of a fragment of SEQ ID NO:23. Applicants disagree that this reference anticipates the claimed invention. Firstly, claim 54 as amended no longer includes part (b), and therefore, no longer encompasses fragments or complementary fragments such as the sequence taught in AI024421. Secondly, as taught in the

specification and claims, the nucleic acid molecules of independent claim 56 were not intended to encompass the nucleic acid sequence as represented in AI024421. In fact, sequences such as AI024421, were specifically stated to be outside the boundaries of the claim. Claim 56 encompasses "unique fragments" taught in the specification on page 19 to be fragments that "...exclude fragments completely composed of the nucleotide sequences of any of GenBank accession numbers listed in Table 8 or other previously published sequences as of the filing date of the priority documents for sequences listed in a respective priority document or the filing date of this application...." AI024421 was listed in Table 8. Accordingly, as the claims are intended to be read in light of the specification, the Applicants assert that the sequence taught in AI024421 was never included in the boundaries of the claims. In order to expedite prosecution of the application, a limitation excluding this specific sequence from the subject matter of claim 56 was added. Support for adding this accession number to the claim can be found in Table 8 of the specification.

Accordingly, in view of the claim amendments and reasoned statements above, Applicants respectfully request the Examiner reconsider and withdraw the rejections made under 35 U.S.C. § 102(b).

CONCLUSION

Applicant submits that this application is in condition for allowance. Favorable consideration and prompt allowance of claims 15, 19, 41, 54, 56, 60, 62, 63, and 76 are requested.

Should the Examiner believe that anything further is desirable to place the application in better condition for allowance, the Examiner is invited to contact the Applicant's undersigned representative at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

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MARKED-UP CLAIMS

15. (Amended) A pharmaceutical preparation comprising

an agent which when administered to the subject enriches selectively the presence of complexes of a MHC molecule and a cancer associated antigen, and

a pharmaceutically acceptable carrier, wherein the cancer associated antigen is a fragment of a cancer associated antigen precursor encoded by a nucleic acid molecule comprising a [NA Group 1 molecule.] nucleic acid molecule selected from the group consisting of (a) nucleic acid molecules which hybridize under stringent conditions to a molecule consisting of a nucleic acid sequence as set forth as SEQ ID NO:23 and which codes for a cancer associated antigen precursor, (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code, and (c) complements of (a) or (b).

19. (Amended) The pharmaceutical preparation of claim 15, wherein the agent is selected from the group consisting of

[(1) an isolated polypeptide comprising the cancer associated antigen, or a functional variant thereof,

(2)] an isolated nucleic acid operably linked to a promoter for expressing the isolated polypeptide, [or functional variant thereof,] and

[(3)] a host cell expressing the isolated polypeptide[, or functional variant thereof, and

(4) isolated complexes of the polypeptide, or functional variant thereof, and a MHC molecule].

41. (Amended) A pharmaceutical composition comprising an isolated nucleic acid molecule selected from the group consisting of [NA Group 1 molecules and NA Group 2 molecules,] (a) nucleic acid molecules which hybridize under stringent conditions to a molecule consisting of a nucleic acid sequence as set forth as SEQ ID NO:23 and which codes for a cancer associated antigen precursor, (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code, (c) complements of (a) or (b), and (d) fragments of (a), (b) or (c), which code for a polypeptide which, or a portion of which, binds an

MHC molecule to form a complex recognized by an autologous antibody or lymphocyte, and a pharmaceutically acceptable carrier.

54. (Amended) An isolated nucleic acid molecule comprising a [NA Group 3]nucleic acid molecule selected from the group consisting of (a) nucleic acid molecules which hybridize under stringent conditions to a molecule consisting of a nucleic acid sequence as set forth as SEQ ID NO:23, and which codes for a cancer associated antigen precursor, (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code, and (c) complements of (a) or (b).

56. (Amended) An isolated nucleic acid molecule selected from the group consisting of

(a) a fragment of a nucleic acid molecule having a nucleotide sequence [selected from the group consisting of nucleotide sequences] as set forth as SEQ ID NO[s. 9, 13, 15, 17, 19, and]:23, of sufficient length to represent a sequence unique within the mouse or human genomes, and [identifying]which identifies it as a nucleic acid encoding a cancer associated antigen precursor,

(b) complements of (a),

provided that the [fragment]isolated nucleic acid molecule includes a sequence of contiguous nucleotides which is not identical to [any sequence selected from the sequence group consisting of

(1) sequences having the GenBank accession numbers of Table 8,

(2) complements of (1), and

(3) fragments of (1) and (2).]the nucleic acid sequence represented by GenBank accession number AI024421.

62. (Amended) An expression vector comprising a [NA Group 1 or Group 2] nucleic acid molecule of any one of claims 15, 41 or 56 and a nucleic acid encoding a MHC molecule.

76. (Amended) A kit for detecting the presence of the expression of a cancer associated antigen precursor comprising

a pair of isolated nucleic acid molecules each of which consists essentially of a molecule selected from the group consisting of (a) a 12-32 nucleotide contiguous segment of the nucleotide sequence [of any of the NA Group 1 molecules] of a nucleic acid molecule which hybridizes under stringent conditions to a molecule consisting of a nucleic acid sequence as set forth as SEQ ID NO:23 and which codes for a cancer associated antigen precursor, (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code and [(b)] (c) complements of (a), wherein the contiguous segments are non-overlapping.